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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,521	09/29/2006	Chac-Ok Yun	P10026US	1275

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EXAMINER	
HILL, KEVIN KAI	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
04/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,521	YUN ET AL.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

Applicant's response to the Requirement for Restriction, filed on April 16, 2009 is acknowledged.

Applicant has elected the invention of Group III, claim(s) 7 and 13, drawn to methods of delivering a gene into cells and treating a cancer, the methods comprising administering a gene delivery system comprising a Relaxin-encoding nucleotide sequence.

Amendments

Applicant's response and amendments, filed February 4, 2010, to the prior Office Action is acknowledged. Applicant has cancelled Claims 1-16 and added new claims, Claims 17-26.

Claims 17-26 are under consideration.

Priority

This application is a 371 of PCT/KR05/00921 filed on March 30, 2005. Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Acknowledgment is made of Applicant's claim for foreign priority based on an application filed in The Republic of Korea on March 30, 2004. It is noted, however, that Applicant has not filed a certified copy of the KR 10-2004-0021601 application as required by 35 U.S.C. 119(b).

Response to Amendment

The Examiner acknowledges Applicant's filing of a certified copy of KR 10-2004-0021601 and a certified translation of the foreign priority document in the papers filed February 4, 2010. The Bibliographic Data Sheet has been updated accordingly.

Examiner's Note

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the February 4, 2010 response will be addressed to the extent that they apply to current rejection(s).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

1. **Claims 17-23 are rejected under 35 U.S.C. 102(b) and 35 U.S.C. 102(e)** as being anticipated by Hirsch et al (U.S. 2003/0003583).

With respect to Claims 17 and 23, Hirsch et al disclose a method of delivering a gene into cells for the treatment of cancer [0151], the method comprising the use of an adenoviral gene delivery system [0019], wherein the gene may encode Relaxin [0140].

With respect to Claims 18-19, the cells are in a tissue composed of cells interconnected with each other by an extracellular matrix, e.g. connective tissue [0013, 0038].

The methodology and compositions may be used for the treatment of a wide variety of conditions, e.g. treatment of cancer [0151], wherein the target protein may have antitumor function [0057].

With respect to the intended use limitations "to enhance a transduction efficiency" (Claim 17) and "enhances… penetration potency...and apoptosis... (Claim 23), such are considered functional properties inherent to the Relaxin protein expressed by the gene delivery system, absent evidence to the contrary. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See MPEP §2114.

"Products of identical chemical composition can not have mutual exclusive properties." A compound and its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure [Relaxin protein encoded by a relaxin gene], the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705,709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP §2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

The mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

Since the Patent Office does not have the facilities for examining and comparing Applicant's relaxin-encoding gene delivery system with the relaxin-encoding gene delivery

system of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed relaxin-encoding gene delivery system and the relaxin-encoding gene delivery system of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

With respect to Claims 20-21, the expression vector is a recombinant adenovirus viral vector [0019].

Response to Arguments

Applicant argues that Hirsch et al. do not disclose a gene delivering method using the construct comprising "a nucleotide sequence of interest to be delivered and a relaxin-encoding nucleotide sequence," as required by present claim 17.

Applicant's argument(s) has been fully considered, but is not persuasive. Hirsch et al disclose adeno-associated viral vectors for transduction of a target gene (Abstract), wherein the target gene may be relaxin [0140].

Applicant argues that the description of relaxin at paragraph [0140] of Hirsch et al only suggests a possible use of relaxin in the method disclosed therein, as a potential "target gene".

Applicant's argument(s) has been fully considered, but is not persuasive. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied,* 493 U.S. 975 (1989). However, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). In the instant case, Hirsch et al disclose adeno-associated viral vectors for transduction of a target gene (Abstract), wherein the target gene may be relaxin [0140].

Applicant argues that Hirsch et al do not disclose "a novel use of relaxin to enhance a transduction efficiency of a target nucleotide sequence," as required by present claim 17. The description of relaxin at paragraph [0140] of Hirsch et al only suggests a possible use of relaxin

in the method disclosed therein, as a potential "target gene," but not for the use to enhance a transduction efficiency of a target gene. No teaching or suggestion of the use of relaxin to enhance a transduction efficiency of a target gene is found in Hirsch et al. Hirsch et al also fails to disclose a method for treating cancers where relaxin is used to enhance a penetration potency of a recombinant adenovirus into a tumor tissue and apoptosis of a tumor cell infected with the recombinant adenovirus.

Applicant's argument(s) has been fully considered, but is not persuasive. Such properties, e.g. "enhance efficiency", are considered functional properties inherent to the Relaxin protein expressed by the gene delivery system, absent evidence to the contrary.

"Products of identical chemical composition can not have mutual exclusive properties." A compound and its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure [Relaxin protein encoded by a relaxin gene], the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705,709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP §2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

The mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

Since the Patent Office does not have the facilities for examining and comparing Applicant's relaxin-encoding gene delivery system with the relaxin-encoding gene delivery system of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed relaxin-encoding gene delivery system and the relaxin-encoding gene delivery system of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Applicant argues that Hirsch et al do not disclose that the recombinant adenoassociated virus carrying the relaxin gene is useful in treating cancers.

Applicant's argument(s) has been fully considered, but is not persuasive. Hirsch et al disclose a method of delivering a gene into cells for the treatment of cancer [0151], the method comprising the use of an adenoviral gene delivery system [0019], wherein the gene may encode Relaxin [0140]. The methodology and compositions may be used for the treatment of a wide variety of conditions, e.g. treatment of cancer [0151], wherein the target protein may have antitumor function [0057].

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. **Claims 22 and 24-26 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Hirsch et al (U.S. 2003/0003583) in view of Hallenbeck et al (U.S. Patent 5,998,205) and Dalemans et al (U.S. Patent 6,136,594).

Determining the scope and contents of the prior art.

Hirsch et al do not disclose the recombinant adenovirus comprises a deleted E3 region into which the relaxin-encoding nucleotide sequence is inserted, an active E1A gene, and/or inactivated E1B 19 gene and/or inactivated E1B 55 gene.

However, at the time of the invention, Hallenbeck et al disclosed recombinant adenoviral expression vectors comprising a deleted E3 region in which the gene of interest to be expressed is inserted (col. 22, line 66-col. 23, line 4), said vector comprises an active E1a gene (col. 5, line 62) operably linked to a heterologous, tissue-specific transcriptional regulatory sequence. Adenovirus vectors are generally deleted in the E1 region of the virus (col. 3, lines 3-5).

Dalemans et al disclosed replication deficient adenovirus vectors in which the majority of E1B genes [which reasonably embraces inactivation of the E1B 19 and/or E1B 55 genes] and E3 region are inactivated (col. 5, lines 25-28).

Ascertaining the differences between the prior art and the claims at issue, and Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as medical doctors, scientists, or engineers possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in molecular biology and the creation of adenoviral expression vectors. Therefore, the level of ordinary skill in this art is high.

"A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1397 (2007). "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* Office personnel may also take into account "the

inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at ___, 82 USPQ2d at 1396.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to substitute a first adenovirus expression vector as taught by Hirsch et al with a second adenovirus expression vector comprising a deletion of the E3 region into which the relaxin-encoding nucleotide is inserted, inactivation of the E1B 19 and/or E1B 55 genes, and/or an active E1A gene as taught by Hallenbeck et al and Dalemans et al with a reasonable expectation of success because the simple substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. M.P.E.P. §2144.07 states "The selection of a known material based on its suitability for its intended use supported a *prima facie* obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)." When substituting equivalents known in the prior art for the same purpose, an express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). M.P.E.P. §2144.06.

An artisan would be motivated to substitute a first adenovirus expression vector with a second adenovirus expression vector comprising a deletion of the E3 region into which the relaxin-encoding nucleotide is inserted, inactivation of the E1B 19 and/or E1B 55 genes, and/or an active E1A gene because those of ordinary skill in the art recognize that the E1A product is required to transcriptionally activate viral and cellular genes (Dalemans; col. 7, lines 53-55) thereby creating a replication-incompetent adenovirus expression vector or a selectively-replicating adenovirus expression vector (Dalemans, Hallenbeck) as per the arbitrary needs [design choice] of the artisan, and Hallenbeck et al successfully demonstrate the use of such modified adenoviral backbones to express a heterologous gene of interest.

The cited prior art meets the criteria set forth in both *Graham* and *KSR*, and the teachings of the cited prior art provide the requisite teachings and motivations with a clear, reasonable

expectation of success. Thus, absent evidence to the contrary, the invention as a whole is *prima facie* obvious.

Conclusion

3. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/
Examiner, Art Unit 1633